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Award Number: DAMD17-99-1-9498

TITLE: SPECT and fMRI Analysis of Motor and Cognitive Indices of Early Parkinson's Disease: The Relationship of Striatal Dopamine and Cortical Function

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REPORT DATE: October 2002

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	October 2002	Annual (1 Oct 01 - 30 Sep 02)

4. TITLE AND SUBTITLE
SPECT and fMRI Analysis of Motor and Cognitive Indices of Early Parkinson's Disease: The Relationship of Striatal Dopamine and Cortical Function

5. FUNDING NUMBERS
DAMD17-99-1-9498

6. AUTHOR(S) :
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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT ***(Maximum 200 Words)***

none provided

14. SUBJECT TERMS:
Parkinson's Disease

15. NUMBER OF PAGES
5

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

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USAMRMC Neurotoxin Exposure Treatment Research Program

Grant #:	**DAMD17-99-1-9498**
Principal Investigators:	**John D. E. Gabrieli, Ph.D.** **Glenn T. Stebbins, Ph.D.**
Institution:	**Rush-Presbyterian-St. Luke's Medical Center**
Grant Title:	**SPECT and fMRI Analysis of Motor and Cognitive Indices of Early Parkinson's Disease: The Relationship of Striatal Dopamine and Cortical Function**

Comments to Previous Annual Report Review

Summary Recommendations, Discrepancies, and/or Technical Assistance

In the previous Annual Report Review, the reviewer suggested interim reports (on a six month basis) be requested by the sponsor to document number of participants screened, number of participants who have agreed to study, number of participants studied, and number of participants scheduled for study. We welcome this suggestion and if agreeable to the sponsor will institute this procedure. In addition, the reviewer suggested investigating the delay in obtaining human subject approval from the USAMRMC HSRRB. This delay has greatly hampered our progress in achieving the goals of the study resulting in an approximate two year delay.

Progress Report for DAMD17-99-1-9498

We have not met all of the goals for this year. Last year we had not been able to recruit any subjects because of a delay obtaining approval from the Human Subjects Research Review Board of Regulatory Compliance and Quality at the USAMRMC. This delay resulted in many problems in SPECT ligand procurement and obtaining of FDA authorization. Our original identification of potential participants (conducted in Year 1) had to be re-instituted to re-identify current participant sources. Coordination of ligand production and delivery to the Nuclear Medicine Department at our institution also had to be re-arranged.

We have met all regulatory requirements for use of the ligand, and arranged the delivery schedule to our institution. Currently, the ligand is manufactured and labeled with radioactive tracer by Boston Life Sciences and Nordion on Tuesdays. The ligand is shipped overnight for use on Wednesdays. This schedule is available twice a month, so we are coordinating our enrollment with ligand availability. This restriction of ligand availability with result in a maximum of 14 subjects per month undergoing SPECT imaging. This should not interfere with our ability to meet delayed recruitment goals, allowing for a maximum 168 scanning per year.

Our recruitment has begun. We are starting the recruitment of participants with Parkinson's disease (PD). Recruitment is being conducted through the Movement Disorders clinic at Rush-Presbyterian-St. Luke's. The recruitment procedure is as detailed in the proposal under the direction of Dr. Christopher G. Goetz. We started with this cohort because we sought to ensure adequate enrollment of PD participants prior to recruitment of younger and older healthy controls. Recruitment begins with a screening and identification of potential participants. To date, we have screened 12 potential participants, and recruited 10. One of the potential participants was allergic to iodine and one was claustrophobic, both exclusion criteria for participation. Thus, we were able to recruit over 85% of the potential participants. We anticipate this rate of successful recruitment will continue in this cohort. The 10 recruited participants meet our inclusion/exclusion criteria, and fall into the following age strata: 6 in 55 - 64 year of age; 4 in 65 - 74 years of age; 0 in 75 - 84 years of age; and 0 in 85+ years of age. Stratification for severity of Parkinsonian symptoms for the entire cohort is 5 in the lower strata and 5 in the higher strata.

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Screening and recruitment of PD participants continues on an on-going basis. The ligand production schedule is such that our first SPECT scans will be in February 2003 (ligand delivery dates 2/5, 2/12). We anticipate scanning these 10 PD participants at that time.

We have begun recruitment of the older healthy control participants (ONC). These potential participants are being recruited from the Memory Assessment Project under the direction of Dr. David Bennett. Because of the delay in approval, we had to re-initiate screening of participants and identification of sites. We have chosen to use the Rush Alzheimer's Disease Center site for two reasons. First, this site has a large cohort of healthy older controls who have agreed to be contacted regarding participation in research projects, including neuroimaging studies. This will facilitate recruitment. Second, these participants are familiar with the location and layout of Rush. The ONC participants will be recruited in February for March scanning (March ligand delivery dates 3/5. 3/12).

We have begun recruitment of the younger healthy control participants (YNC). Currently, we have recruited three of the 20 participants. We plan on scanning using these participants to fill-out the scanning schedule in February, but may continue them into March.

Development of a Novel Scanning Paradigm for Assessment of White Matter Integrity

We continue to develop Diffusion Tensor Imaging in PD. Specifically, we have completed two studies investigating white matter pathology in PD. The first was presented at the 2002 American Academy of Neurology meetings (Neurology 2002;58(suppl 3):A200) and demonstrated regional decrease in white matter integrity in PD in the frontal forceps, longitudinal fasciculus, and the corticostriate tract in 20 patients with PD and 20 age matched healthy controls. The second study combined DTI white matter assessment with fMRI activation in 15 patients with PD and 15 age matched healthy controls and was presented at the Society for Neuroscience meeting (Program No. 714.11, 2002 Abstract Viewer/Itinerary Planner, Washington, DC: Society for Neuroscience, 2002, CD-ROM). This second paper presented our methods for combining different neuroimaging modalities and thus has direct relevance to the present project.

Regulatory Issues

In anticipation of HIPAA regulation initiation on April 14,2003, all study personnel have either received or will receive HIPAA training through the Office of Research Affairs (ORA) at Rush-Presbyterian-St. Luke's Medical Center. We will add a HIPAA authorization form to all consents signed after April 13, 2003 when the ORA makes that form available. Approval from the sponsor will be obtained prior to including HIPAA authorization.

If you have comments or questions regarding this Annual Progress Report, please contact me via mail (Glenn T. Stebbins, Ph.D., Department of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, 1725 W. Harrison, Suite 309, Chicago, IL 60612), telephone ((312) 563-3854), or electronic mail (gstebbin@rush.edu).

Respectfully submitted,

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